



## **Genmab Announces AbbVie Receives Positive CHMP Opinion for Epcoritamab (TEPKINLY®) for the Treatment of Adults with Relapsed/Refractory (R/R) Diffuse Large B-cell Lymphoma (DLBCL)**

July 21, 2023

### **Company Announcement**

- **The positive CHMP opinion is supported by results from the EPCORE™ NHL-1 phase 1/2 trial evaluating the preliminary efficacy and safety of epcoritamab in patients with non-Hodgkin's lymphoma (NHL), including diffuse large B-cell lymphoma (DLBCL)**
- **DLBCL is an aggressive subtype of NHL and accounts for approximately 30 percent of all global cases**
- **If approved, epcoritamab (TEPKINLY®) would become the first and only subcutaneous bispecific antibody conditionally approved as a monotherapy in the European Union for the treatment of adult patients with relapsed or refractory (R/R) DLBCL after two or more lines of systemic therapy**

**COPENHAGEN, Denmark; July 21, 2023** – [Genmab A/S \(Nasdaq: GMA\)](#) today announced that the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion recommending the granting of conditional marketing authorization of epcoritamab (TEPKINLY®) as a monotherapy for the treatment of adult patients with relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy. The final European Commission decision on the indication for epcoritamab is anticipated later this year.

"Today's CHMP opinion is an important step forward in our mission to bringing innovative, readily available medicines like epcoritamab to patients in Europe who are in need of alternative treatment options for relapsed or refractory diffuse large B-cell lymphoma," said Jan van de Winkel, Ph.D., Chief Executive Officer of Genmab. "We look forward to continuing our work with AbbVie to develop epcoritamab as a potential core therapy across B-cell malignancies."

AbbVie's application for the approval of epcoritamab is supported by results from the pivotal EPCORE™ NHL-1 phase 1/2 open-label, multi-center trial evaluating the safety and preliminary efficacy of epcoritamab in patients with relapsed, progressive or refractory CD20+ mature B-cell NHL, including DLBCL. The primary endpoint of the study was overall response rate, as assessed by an independent review committee (63.1 percent). The most common treatment-emergent adverse event was cytokine release syndrome.<sup>i</sup> Updated results were recently presented at multiple medical congresses.

"Diffuse large B-cell lymphoma is an aggressive and often treatment-resistant disease with limited therapeutic options for patients whose disease is refractory or who have experienced relapse after multiple lines of therapy," said Catherine Thieblemont, M.D., Ph.D., head of the hemato-oncology department, Paris University, Hôpital Saint-Louis Assistance-Publique-Hopitaux de Paris (APHP) in Paris. "Subcutaneous epcoritamab could become a promising treatment option for the DLBCL community, and I look forward to the European Commission's final decision."

DLBCL is an aggressive type of cancer that develops in the lymphatic system. It is the most common type of B-cell NHL worldwide and accounts for approximately 30 percent of all global cases. Because NHL affects B-cell lymphocytes, the disease and its subtypes, including DLBCL, are classified as B-cell malignancies.<sup>ii</sup>

Epcoritamab is being co-developed by Genmab and AbbVie as part of the companies' oncology collaboration. The companies will share commercial responsibilities in the U.S. and Japan, with AbbVie responsible for further global commercialization.

### **About the EPCORE™ NHL-1 Trial**

EPCORE™ NHL-1 is an open-label, multi-center safety and preliminary efficacy trial of epcoritamab that includes a phase 1 first-in-human, dose escalation part; a phase 2a expansion part; and a dose optimization part. The trial was designed to evaluate subcutaneous epcoritamab in patients with relapsed, progressive or refractory CD20+ mature B-cell NHL, including large B-cell lymphoma (LBCL) and DLBCL.<sup>iii</sup> Data from the dose escalation part of the study, which determined the recommended phase 2 dose, were published in September 2021.<sup>iv</sup> In the phase 2 expansion part, additional patients were treated with epcoritamab to further explore the safety and efficacy of epcoritamab in three cohorts of patients with different types of relapsed/refractory B-cell NHLs who had limited therapeutic options.<sup>iii</sup>

The primary endpoint of the phase 2 expansion part was overall response rate as assessed by an independent review committee. Secondary efficacy endpoints included duration of response, complete response rate, progression-free survival, overall survival, time to response, time to next therapy, and rate of minimal residual disease negativity. The most common treatment-emergent adverse events were cytokine release syndrome (49.7 percent; grade 1 or 2: 47.1 percent; grade 3: 2.5 percent), pyrexia (23.6 percent) and fatigue (22.9 percent). Results from the phase 2 expansion part of the study were published in December 2022.<sup>i</sup> More information can be found on [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

### **About Epcoritamab**

Epcoritamab is an investigational IgG1-bispecific antibody created using Genmab's proprietary DuoBody® technology and administered subcutaneously. Genmab's DuoBody®-CD3 technology is designed to direct cytotoxic T-cells selectively to elicit an immune response toward target cell types. Epcoritamab is designed to simultaneously bind to CD3 on T-cells and CD20 on B-cells and induces T-cell mediated killing of CD20+ cells.<sup>v</sup>

CD20 is expressed on B-cells and is a clinically validated therapeutic target in many B-cell malignancies, including DLBCL, follicular lymphoma, mantle cell lymphoma and chronic lymphocytic leukemia.<sup>vi,vii</sup>

The safety and efficacy of epcoritamab remain under evaluation in the European Union. Epcoritamab-bysp (EPKINLY<sup>TM</sup>) was recently approved in the United States and is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified (NOS), including DLBCL arising from indolent lymphoma, and high-grade B-cell lymphoma (HGBL) after two or more lines of systemic therapy. This indication is approved under accelerated approval based on response rate and durability of response. Continued approval for this indication is contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Epcoritamab is not approved in the European Union. If approved, epcoritamab will be marketed under the brand name TEPKINLY<sup>®</sup> in all EU member states plus Liechtenstein, Norway and Iceland. AbbVie will continue to pursue regulatory submissions for epcoritamab across international markets throughout the year.

## **EPKINLY<sup>TM</sup> (epcoritamab-bysp) U.S. IMPORTANT SAFETY INFORMATION**

### **Important Warnings—EPKINLY can cause serious side effects, including:**

- **Cytokine Release Syndrome (CRS).** CRS is common during treatment with EPKINLY and can be serious or life-threatening. Tell your healthcare provider or get medical help right away if you develop symptoms of CRS, including fever of 100.4°F (38°C) or higher, dizziness or lightheadedness, trouble breathing, chills, fast heartbeat, feeling anxious, headache, confusion, shaking (tremors), or problems with balance and movement, such as trouble walking.

**Due to the risk of CRS, you will receive EPKINLY on a "step-up" dosing schedule.** The step-up dosing schedule is when you receive smaller "step-up" doses of EPKINLY on day 1 and day 8 of your first cycle of treatment (cycle 1). You will receive your first full dose of EPKINLY on day 15 of cycle 1. If your dose of EPKINLY is delayed for any reason, you may need to repeat the step-up dosing schedule. Before each dose in cycle 1, you will receive medicines to help reduce your risk of CRS. Your healthcare provider will decide if you need to receive medicine to help reduce your risk of CRS with future cycles.

- **Neurologic problems.** EPKINLY can cause serious neurologic problems that can be life-threatening and lead to death. Neurologic problems may happen days or weeks after you receive EPKINLY. Your healthcare provider may refer you to a healthcare provider who specializes in neurologic problems. Tell your healthcare provider right away if you develop any symptoms of neurologic problems, including trouble speaking or writing, confusion and disorientation, drowsiness, tiredness or lack of energy, muscle weakness, shaking (tremors), seizures, or memory loss.

**Due to the risk of CRS and neurologic problems,** you should be hospitalized for 24 hours after receiving your first full dose of EPKINLY on day 15 of cycle 1. Your healthcare provider will monitor you for symptoms of CRS and neurologic problems during treatment with EPKINLY, as well as other side effects, and treat you if needed. Your healthcare provider may temporarily stop or completely stop your treatment with EPKINLY if you develop CRS, neurologic problems, or any other side effects that are severe.

**Do not** drive or use heavy or potentially dangerous machinery if you develop dizziness, confusion, tremors, drowsiness, or any other symptoms that impair consciousness until your symptoms go away. These may be symptoms of CRS or neurologic problems.

### **EPKINLY can also cause other serious side effects, including:**

- **Infections.** EPKINLY can cause serious infections that may lead to death. Your healthcare provider will check you for symptoms of infection before and during treatment. Tell your healthcare provider right away if you develop any symptoms of infection during treatment, including fever of 100.4°F (38°C) or higher, cough, chest pain, tiredness, shortness of breath, painful rash, sore throat, pain during urination, or feeling weak or generally unwell.
- **Low blood cell counts.** Low blood cell counts are common during treatment with EPKINLY and can be serious or severe. Your healthcare provider will check your blood cell counts during treatment. EPKINLY may cause low blood cell counts, including **low white blood cell counts (neutropenia)**, which can increase your risk for infection; **low red blood cell counts (anemia)**, which can cause tiredness and shortness of breath; and **low platelet counts (thrombocytopenia)**, which can cause bruising or bleeding problems.

Your healthcare provider may temporarily stop or completely stop treatment with EPKINLY if you develop certain side effects.

### **Before you receive EPKINLY, tell your healthcare provider about all of your medical conditions, including if you:**

- have an infection.
- are pregnant or plan to become pregnant. EPKINLY may harm your unborn baby. **Females who are able to become pregnant:** Your healthcare provider should do a pregnancy test before you start treatment with EPKINLY. You should use effective birth control (contraception) during treatment and for 4 months after your last dose of EPKINLY. Tell your healthcare provider if you become pregnant or think that you may be pregnant during treatment with EPKINLY.
- are breastfeeding or plan to breastfeed. It is not known if EPKINLY passes into your breast milk. Do not breastfeed during treatment with EPKINLY and for 4 months after your last dose of EPKINLY.

**Tell your healthcare provider about all of the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

**The most common side effects of EPKINLY** include CRS, tiredness, muscle and bone pain, injection site reactions, fever, stomach-area (abdominal) pain, nausea, and diarrhea.

These are not all the possible side effects of EPKINLY. Call your doctor for medical advice about side effects.

You are encouraged to report side effects to the FDA at (800) FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch) or to Genmab US, Inc. at 1-855-4GENMAB (1-855-443-6622).

Please see the [Full Prescribing Information](#) and [Medication Guide](#), including Important Warnings.

#### About Genmab

Genmab is an international biotechnology company with a core purpose guiding its unstoppable team to strive towards improving the lives of patients through innovative and differentiated antibody therapeutics. For more than 20 years, its passionate, innovative and collaborative team has invented next-generation antibody technology platforms and leveraged translational research and data sciences, which has resulted in a proprietary pipeline including bispecific T-cell engagers, next-generation immune checkpoint modulators, effector function enhanced antibodies and antibody-drug conjugates. To help develop and deliver novel antibody therapies to patients, Genmab has formed 20+ strategic partnerships with biotechnology and pharmaceutical companies. By 2030, Genmab's vision is to transform the lives of people with cancer and other serious diseases with Knock-Your-Socks-Off (KYSO) antibody medicines.

Established in 1999, Genmab is headquartered in Copenhagen, Denmark with locations in Utrecht, the Netherlands, Princeton, New Jersey, U.S. and Tokyo, Japan. For more information, please visit [Genmab.com](http://Genmab.com) and follow us on [Twitter.com/Genmab](https://twitter.com/Genmab).

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<sup>i</sup> Thieblemont C, Phillips T, Ghesquieres H, et al. Epcoritamab, a Novel, Subcutaneous CD3xCD20 Bispecific T-Cell–Engaging Antibody, in Relapsed or Refractory Large B-Cell Lymphoma: Dose Expansion in a Phase I/II Trial. JCO. Published online December 22, 2022;JCO.22.01725. doi:10.1200/JCO.22.01725.

<sup>ii</sup> Sehn, Salles. "Diffuse Large B-Cell Lymphoma." N Engl J Med. 2021;384:842-858. DOI: 10.1056/NEJMra2027612.

<sup>iii</sup> First-in-human (FIH) trial in patients with relapsed, progressive or refractory B-cell lymphoma - clinicaltrials.gov. in. (n.d.). <https://classic.clinicaltrials.gov/ct2/show/NCT03625037>. Accessed July 5, 2023.

<sup>iv</sup> Hutchings M, Mous R, Roost Clausen M, et al. Dose escalation of subcutaneous epcoritamab in patients with relapsed or refractory B-cell non-Hodgkin lymphoma: an open-label, phase 1/2 study. The Lancet. Published Online September 8, 2021;volume 398, Issue 10306, P-1157-1169.

<sup>v</sup> Engelberts et al. "DuoBody-CD3xCD20 induces potent T-cell-mediated killing of malignant B cells in preclinical models and provides opportunities for subcutaneous dosing." EBioMedicine. 2020;52:102625. DOI: 10.1016/j.ebiom.2019.102625.

<sup>vi</sup> Rafiq, Butchar, Cheney, et al. "Comparative Assessment of Clinically Utilized CD20-Directed Antibodies in Chronic Lymphocytic Leukemia Cells Reveals Divergent NK Cell, Monocyte, and Macrophage Properties." J. Immunol. 2013;190(6):2702-2711. DOI: 10.4049/jimmunol.1202588.

<sup>vii</sup> Singh, Gupta, Almasan. "Development of Novel Anti-Cd20 Monoclonal Antibodies and Modulation in Cd20 Levels on Cell Surface: Looking to Improve Immunotherapy Response." J Cancer Sci Ther. 2015;7(11):347-358. DOI: 10.4172/1948-5956.1000373.

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**Attachment**

- [190723-ca35-epcoritamab-DLBCL-CHMP Opinion](#)